POSTER BOARD NUMBER P4 – 291

2241 EFFECT OF GENETIC POLYMORPHISMS OF MRP2 AND UGT2B7 ON GASTROINTESTINAL SYMPTOM RATING SCALE IN KIDNEY TRANSPLANT RECIPIENTS TAKING MYCOPHENOLIC ACID

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Background: Gastrointestinal (GI) symptoms are the most common complications with mycophenolic acid (MPA) therapy. MRP2 and UGT2B7 which are involved in the excretion and production of the metabolites of MPA respectively may play a role in the presentation of GI symptoms.

Objectives: To determine the relationship between single nucleotide polymorphisms in MRP2 and UGT2B7 and the incidence and severity of the GI symptoms in patients receiving MPA. Methods: Genotypes of MRP2 C-24T and UGT2B7 C802T were determined and the incidence and severity of GI symptoms were assessed using the validated Gastrointestinal Symptom Rating Scale (GSRS) at baseline, 2 weeks, 1 month, 3 months and 6 months post transplant. The mean overall GSRS score and subscale score for diarrhea were compared using Student’s t-test and linear regression was performed to determine the predictors of GI symptoms.

Results: Fifty-six kidney transplant recipients were included in the study. The overall GSRS score was not significantly different between the MRP2 C-24T heterozygous variant and the homozygous wild type (1.6 vs 1.8, p=0.084). However the GSRS subscale score for diarrhea was significantly lower in the MRP2 C-24T heterozygous variant compared to the homozygous wild type (1.2 vs 1.7, p=0.004). For the UGT2B7 C802T, the overall GSRS score (1.6 vs 1.8, p=0.158) and diarrhea subscale score (1.4 vs 1.8, p=0.127) were not significantly different between the heterozygous variant and the homozygous wild type. When the genotypes for MRP2 and UGT2B7 are considered together, the variant MRP2 C-24T and UGT2B7 C802T had significantly lower overall GSRS (1.5 vs 1.9, p=0.032) and diarrhea subscale score (1.1 vs 1.8, p=0.014) compared to the wild type. There were however no differences in the scores between patients receiving either mycophenolate mofetil or enteric-coated mycophenolate sodium; and patients receiving the different calcineurin inhibitors.

Conclusion: This study demonstrates that among patients receiving MPA, those with MRP2 C-24T and UGT2B7 C802T variant genotypes are potentially protected from the GI side effects, in particular diarrhea, regardless of the formulation administered.

POSTER BOARD NUMBER P4 – 292

2242 SYSTEMS BIOLOGY IN DONOR KIDNEYS OF RECIPIENTS WITH POST-TRANSPLANT ANEMIA

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Post-Transplantation anemia is a common phenomenon after renal transplantation, and the cause is usually multi-factorial. Molecular mechanisms leading to anemia after renal transplantation are not fully understood. Focus of this present study was to further elucidate the biological processes of anemia in the post-transplantation setting.

The analysis of 52 renal transplant recipients (25 treated with ESAs within the first year after transplantation and 27 without ESA treatment) will be presented. The analysis include genome-wide gene expression profiles of donor kidney biopsies with subsequent systems biology approaches such as transcription factors analysis, regulatory networks, and protein-protein interaction data. Multivariable logistic regression analysis was used to quantify the association of genes identified in the systems biology studies with the outcome ESA use adjusted for clinical predictors such as donor age, biopsy confirmed acute rejection (BCAR) and glomerular filtration rate. Unsupervised hierarchical clustering of experimental data suggests a distinct molecular signature associated with activated inflammation in the donor kidney biopsies with subsequent ESA requirement. Selection of 1,560d differentially upregulated genes in the ESA group yielded 28 significant sequences that can be categorized according to PANTHER ontologies into three main biological processes: Cell adhesion-mediated signalling (p<0.004), immunity and defense (p<0.004), oncogenesis (p<0.007). In the multivariable analysis, several genes were found to be independent predictors of post-transplant anemia.

Our data suggest that genes involved in the inflammation cascade predict post-transplant anemia.

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